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British Association of Dermatologists' guidelines for the management of lichen sclerosus 2010

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None declared.

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One of the aims of the British Association of Dermatologists (BAD) is to provide guidelines for the management of skin diseases using all available good-quality evidence-based data. The BAD guidelines writing and consultation process, and its revised formats, have been described elsewhere.[1–3]

These guidelines for the management of lichen sclerosus (LS) have been prepared for dermatologists on behalf of the BAD. They present evidence-based guidance for investigation and treatment, with identification of the strength of evidence available at the time of preparation of the guidelines.

Purpose and scope

The guidelines have been revised and updated in accordance with a predetermined scope, based on that used in the 2002 guidelines. Recommendations in these guidelines supersede those in the 2002 guidelines. The overall objective of the guidelines is to provide up-to-date recommendations for the management of LS in adults and children.

Stakeholder involvement

This guidance has been written by dermatologists and has been shown to a patient. The guidelines have also been seen by a urologist, gynaecologist and genitourinary physician, all of whom are involved in the management of patients with LS.

Methodology

These guidelines have been developed using the BAD's recommendations[3] and also with reference to the AGREE (Appraisal of Guidelines Research and Evaluation) instrument.[4] Medline and EMBASE databases were searched from 2002 to 2009 and full relevant papers obtained. The draft guidelines were made available for consultation and review by the BAD membership; the final document was peer reviewed by the Clinical Standards Unit of the BAD (made up of the Therapy & Guidelines and Audit & Clinical Standards Subcommittees) prior to publication.

There are few published randomized controlled trials to support the following guidelines for the management of LS; the recommendations made are those that are currently con-

sidered best practice but they will be modified at intervals in the light of new evidence. LS, although a dermatosis, occurs commonly at a genital site and consequently is not only managed by dermatologists; patients may be under the care of other specialist disciplines. There have been many long-standing difficulties in the appraisal and grading of the evidence for the treatment of LS. Historically, the nomenclature used to describe LS has been unclear. In addition, there may be difficulty in assessing the number of patients with active disease as, although asymptomatic, there is still ongoing activity as evidenced by scarring. There are also instances where the LS may be in remission but the patient still experiences symptoms due to a secondary sensory disorder, or additional irritant eczema.

Plans for revision

These guidelines will be revised as necessary to reflect changes in practice.

Limitations of the guidelines

These guidelines have been prepared for dermatologists on behalf of the BAD and reflect the best data available at the time the report was prepared. Caution should be exercised in interpreting the data; the results of future studies may require alteration of the conclusions or recommendations in this report. It may be necessary or even desirable to depart from the guidelines in the interests of specific patients and special circumstances. Just as adherence to guidelines may not constitute defence against a claim of negligence, so deviation from them should not necessarily be deemed negligent.

Definition

LS is an autoimmune, inflammatory dermatosis, characterized by a lymphocytic response that has a predilection for the genital skin in both sexes, and an association with several other autoimmune diseases.

The aetiology of LS is uncertain but there is mounting evidence to suggest that autoimmune mechanisms are involved in its pathogenesis;[5–7] there is an increased incidence of tissue-specific antibodies[8] and associations with other autoimmune diseases in patients with LS,[9,10] as well as positive associations with HLA class II antigens.[11–13] There is still controversy regarding the implication of *Borrelia* infection as an aetiological agent; although several studies have shown that this association does not occur in the U.S.A., some doubt still remains in Europe.[14,15] The presence of circulating extracellular matrix protein antibodies gives further support to an immune aetiopathology in female patients.[16] 'Balanitis xerotica obliterans' is now viewed as a synonymous term describing LS of the penis, and 'kraurosis vulvae' is now recognized as LS of the vulva. The term 'leucoplakia' (meaning white plaque) is not a diagnostic entity and is descriptive only, as many conditions may present with white plaques. The term 'lichen sclerosus et atrophicus' has been abbreviated to 'lichen sclerosus' as some cases are associated with a hypertrophic, rather than atrophic, epithelium. There are instances when it can be difficult to differentiate between LS and lichen planus (LP) on the basis of the clinical and histological features; these cases appear to constitute an overlap syndrome, which is often associated with squamous cell hyperplasia and a poor response to ultrapotent topical corticosteroids.

In the main, these guidelines are for classical LS with typical clinical and histological features.

Incidence and patterns

LS is a relatively common dermatosis, although the true incidence is unknown, and probably underestimated, in part due to the distribution of patients among different clinical specialities and to the fact that it may be asymptomatic. Genital LS in female subjects has two peak ages of presentation – in the prepubertal and postmenopausal years.[17] Although childhood LS usually improves, there may be cases that persist into adulthood.[18] There is also a bimodal onset in male subjects, with age peaks in young boys and in adult men.[19]

Clinical features

Readers are referred to several reviews on the clinical, histological and pathogenetic aspects of LS[20–23] and to a historical review of the nomenclature and therapy.[24]

Female anogenital: adult

The typical lesions are porcelain-white papules and plaques, often associated with areas of ecchymosis. Follicular delling may be prominent, and occasionally hyperkeratosis is a prominent feature. The characteristic sites are the interlabial sulci, labia minora, clitoral hood, clitoris, perineal body and perineum. Genital mucosal involvement does not occur, the vagina and cervix always being spared (which is in contrast to LP), although there may be involvement at the mucocutaneous junctions (the vestibule), which may result in introital narrowing. Perianal lesions occur in women in 30% of cases. There may be extension to the buttocks and genitocrural folds. LS can Koebnerize and may first arise in an episiotomy scar.

Itch is the main symptom, but pain may be a consequence of erosions or fissures. However, LS may also be entirely asymptomatic and an incidental finding on examination. In those with itch, this is often worse at night and may be sufficiently severe to disturb sleep. Dyspareunia occurs in the presence of erosions, fissures or introital narrowing.

LS is a scarring process and may cause loss of the labia minora, sealing of the clitoral hood and burying of the clitoris. Severe introital stenosis may rarely occur, but is seen more frequently in the LS/LP overlap syndrome.

Female anogenital: children

The lesions are similar to those in adult women, but ecchymosis may be very striking and potentially mistaken as evidence of sexual abuse.[25] The confirmation of a diagnosis of LS does not, however, totally exclude coincident sexual abuse as some cases of LS may possibly be caused or aggravated by sexual abuse through Koebnerization.[26] Features that should arouse suspicion of this include LS arising in older prepubertal girls, poor response to treatment, the presence of associated sexually transmitted infection or other symptoms or signs of abuse.

Milia may also be present transiently in treated and untreated disease.

Perianal involvement is a frequent finding in young girls, who may present with constipation because of painful fissuring in this area.

Male genital: adult

The common sites of involvement of LS in adult men are the prepuce, coronal sulcus and glans penis, and more rarely lesions may be found on the shaft of the penis. The presenting complaint is usually tightening of the foreskin, which may lead to phimosis. This in turn results in erectile dysfunction and painful erections. One report documents that 30% of phimosis occurring in adults was due to LS,[27] although another study of 75 subjects with severe phimosis identified LS in only 11%.[28] Other presenting complaints are due to the appearance of lesions or changes in urinary stream, but itch is not a prominent symptom. Perianal disease is rarely, if ever, seen in male patients. The perimeatal area may be involved and postinflammatory scarring may lead to stenosis and obstruction. There may also be more proximal urethral involvement although this usually starts at the meatus.[23] These complications may require a multidisciplinary approach with input from both a dermatologist and urologist.

Male genital: children

The disease usually affects the prepuce and the most frequent presentation is phimosis. The reported incidence of LS in children with phimosis ranges from 14% to 100%.[29–31] Perianal involvement, as in adult men, is extremely rare. There is a report of a rare complication of renal failure following meatal obstruction.[32]

Extragenital: male, female and children

The classical sites for extragenital lesions are the upper trunk, axillae, buttocks and lateral thighs, and these are involved most frequently in adult women. Rarer sites include the mouth, face, scalp, hands, feet and nails. The typical lesions are porcelain-white plaques, which may have follicular dells and areas of ecchymosis, similar to the genital lesions. In extragenital sites, there may be difficulty in distinguishing the lesions from those of morphoea. The clinical types of extragenital LS include an extensive bullous form,[33,34] as well as annular, Blaschkoid and keratotic variants.[35] Koebnerization is very common at extragenital sites, arising at pressure points, old surgical and radiotherapy scars and at sites of trauma.

Investigations

Biopsy

A confirmatory biopsy, although ideal, is not always practical, particularly in children. It is not always essential when the clinical features are typical. However, histological examination is advisable if there are atypical features or diagnostic uncertainty and is mandatory if there is any suspicion of neoplastic change. Patients under routine follow-up will need a biopsy if: (i) there is a suspicion of neoplastic change, i.e. a persistent area of hyperkeratosis, erosion or erythema, or new warty or papular lesions; (ii) the disease fails to respond to adequate treatment; (iii) there is extragenital LS, with features suggesting an overlap with morphoea; (iv) there are pigmented areas, in order to exclude an abnormal melanocytic proliferation; and (v) second-line therapy is to be used.

Immunology

An autoantibody screen to look for associated autoimmune disease is useful if there are clinical features to suggest an autoimmune disorder. In particular, thyroid disease is common in women with LS.[36]

Microbiology

Swabs are not required routinely but may be indicated in erosive disease to exclude herpes simplex or *Candida* as additional complicating problems.[37] Retesting for these infections may be necessary in disease that flares or fails to respond to treatment. If there is an abnormal vaginal discharge this will need appropriate investigation.

Complications

Malignancy

Squamous cell carcinoma (SCC) has been described predominantly in association with female genital LS and less commonly in penile LS. It is not associated with extragenital LS. Less commonly the malignancy is a verrucous carcinoma. Melanoma, basal cell carcinoma and Merkel cell carcinoma have all been reported rarely in patients with vulval LS but no studies suggest that there is an increased frequency of these tumours. There appear to be two pathogenetic mechanisms for vulval SCC: firstly, SCC in younger women is associated with the oncogenic human papillomavirus (HPV); and secondly, in older women, the association is with a chronic scarring dermatosis such as LS or LP with little, if any, evidence of a link with HPV.

Squamous cell carcinoma in female patients with genital lichen sclerosus

SCC arising within LS only occurs in anogenital disease. The risk is small, being < 5%.[17,23,38] However, histopathological examination of vulval SCCs indicates that about 60% occur on a background of LS.[39–41] LS may act as both an initiator and promoter of carcinogenesis by mechanisms that seem to be independent of HPV. Although there is little evidence for an important role for HPV in LS-associated SCC, there has been a suggestion that topical corticosteroid use may induce oncogenic HPV types. HPV may be found in vulval intraepithelial neoplasia (VIN) associated with LS.[42] SCC of the vulva should be managed by oncological gynaecologists experienced in this field as surgery has to be individualized according to the tumour size and location, particularly in early invasive disease.

Squamous cell carcinoma in men with genital lichen sclerosus

An association between LS and penile SCC has also been reported.[43–45] Although histological evidence of LS can be found in about 40% of penile carcinoma specimens, the actual risk of this complication in any individual patient with LS is uncertain. Published data suggest that the risk is about 5%, similar to the figure suggested for female patients.[43] In a 10-year multicentre cohort of 130 male patients with genital LS, histological changes of SCC were found in eight, verrucous carcinoma in two and erythroplasia of Queyrat (*in situ* SCC) in one.[46]

The role of HPV in penile LS-associated SCC has also been debated. Some studies using polymerase chain reaction have documented a negligible frequency of HPV in LS,[47,48] but other studies have suggested a frequency of up to 33%.[49,50] An additional feature that has been linked with penile LS-associated SCC is the occurrence of a prominent lichenoid infiltrate on long-standing, chronic LS, suggesting disease reactivation.[51]

Scarring

Introital narrowing

This is rare, but, if significant and causing dyspareunia or difficulty with micturition, surgery may need to be considered. Part of the posterior vaginal wall is used in the reconstruction to prevent further adhesions and stenosis due to Koebnerization.[52]

Pseudocyst of the clitoris

Occasionally, clitoral hood adhesions seal over the clitoris and keratinous debris builds up underneath forming a painful pseudocyst. This requires a subtotal or total circumcision.[53]

Preputial adhesions and phimosis

If subcoronal or transcoronal adhesions between the inner aspect of the prepuce and the glans persist despite adequate medical treatment, these will need to be treated surgically and a circumcision performed at the same time. Persistent phimosis will also require a circumcision. If the disease is still active at the time of surgery a topical steroid might be required to prevent Koebnerization and further scarring, particularly around the coronal sulcus.

Meatal stenosis

If this results in an impaired urinary stream, referral for urological assessment is advisable.

Sensory abnormalities: dysaesthesia

Vestibulodynia and vulvodynia

These conditions may occur after an inflammatory condition of the vulva or vestibule. Typically, the patient remains symptomatic despite objective clinical improvement or resolution of the skin lesions. Neuropathic pain does not respond to topical corticosteroids, and treatment must be directed to the eradication of the neuronal sensitization. Initially, 5% lidocaine ointment is recommended, with the addition of pain-modulating oral medication, such as a tricyclic antidepressant or gabapentin, in unresponsive cases.

Penile dysaesthesia

Men may develop a similar problem, with an abnormal burning sensation on the glans or around the urethral meatus. The management is as for female patients.

Psychosexual problems

Men and women who have any chronic genital disorder will often lose their interest in sexual activity, leading to problems with sexual dysfunction.[54,55] It is important to give the patient the opportunity to express their concerns about their sexual function, and to offer a referral to someone with the necessary expertise to address these problems. Women are more likely to bring up sexual matters if they have seen the doctor before and feel comfortable with the consultation. However, many patients are too embarrassed to bring up the topic of sexual function and it is important that the doctor asks a simple question about sexual activity and associated concerns. Sometimes it is the patient's partner who has a problem and does not wish to have physical contact for fear of hurting the partner or 'catching' the disease.

Management

Topical corticosteroids

Topical steroids have become the mainstay of medical treatment for LS.

Adult female anogenital lichen sclerosus

There are no randomized controlled trials providing evidence that a once- or twice-daily application of any one specific corticosteroid is the most effective, or documenting that one regimen is superior to another. However, the recommended and accepted first-line treatment is the very potent topical corticosteroid clobetasol propionate 0·05%[56–58] (*Strength of recommendation B; quality of evidence* 2++; see Appendix for definitions). The regimen recommended by the authors for a newly diagnosed case is clobetasol propionate 0·05% ointment applied once daily, at night, for 4 weeks, then on alternate nights for 4 weeks, and then twice weekly for a further 4 weeks, before review. The rationale for once-a-day application is based on pharmacodynamic studies showing that an ultrapotent steroid only needs to be applied once a day on extragenital skin.[59] If symptoms recur when the frequency of application is reduced, the patient is instructed to use the treatment more often until the symptoms resolve. They can then try to reduce the frequency again. A 30-g tube of clobetasol propionate 0·05% should last at least 12 weeks. If the treatment has been successful the hyperkeratosis, ecchymoses, fissuring and erosions should have resolved, but the atrophy, scarring and its associated pallor will persist. About 60% of patients experience complete remission of their symptoms.[60,61] Others will continue to have flares and remissions; they are advised to use clobetasol propionate 0·05% as required. Most patients with ongoing disease seem to require 30–60 g of clobetasol propionate 0·05% ointment annually. In our experience, the long-term use of clobetasol propionate in this way is safe and there has been no evidence of significant steroid damage or an increase in the incidence of SCC. There is one short-term study of up to 12 months showing the safety of continued use.[62]

One study using the less potent steroid mometasone furoate showed that this was also effective.[63]

A prospective open study of 34 postmenopausal women with vulval LS demonstrated that the use of an emollient, in addition to the topical steroid during the initial treatment phase, and then as maintenance therapy, is very beneficial.[64] No patients had worsening of scarring during follow-up. A soap substitute is also recommended.

An information sheet on LS, with the instructions for the use of the topical steroid, should be given to the patient.

Adult male genital lichen sclerosus

A retrospective study of 22 men treated with clobetasol propionate 0·05% documented this to be safe and effective, with significant improvement in discomfort and skin tightness, and also in urinary flow in the nine patients in whom this was affected.[65] The use of topical steroids in men may also reduce the need for circumcision[66] (*Strength of recommendation B; quality of evidence* 2++).

Child anogenital lichen sclerosus

There are no ongoing randomized controlled trials to base the recommendation of a potent topical corticosteroid as being the treatment of choice for childhood LS in either sex. In a series of 70 cases of childhood vulval LS, potent topical corticosteroids were effective treatment to alleviate symptoms, without significant side-effects.[67] Several smaller series support this conclusion.[68,69] A prospective study, completed by 111 boys with phimosis using betamethasone for 1 month, documented that 80% had normal retractability of the foreskin after this time, 10% proceeded to circumcision as treatment failures and 10% required ongoing topical treatment.[70] One placebo-controlled series using a medium potency steroid documented improvement in disease with little scarring.[71] Other studies have shown that preputial phimosis may resolve with the use of an ultrapotent or medium potency topical steroid, thus avoiding a need for circumcision.[72,73] Interestingly, in a series of 462 boys with phimosis, only 12 of whom had documented LS, 86% responded to twice-daily corticosteroid application for 6 weeks, but only nine of the patients with LS responded:[74] this suggests that phimosis due to causes other than LS may also respond to topical corticosteroids (*Strength of recommendation B; quality of evidence* 2++).

Extragenital LS

There are no randomized controlled trials on which to base recommendations but clobetasol propionate, with or without occlusion, is used once daily as and when required. In general, extragenital lesions are not as responsive as genital disease to topical corticosteroid therapy.

Testosterone and other hormonal treatments

Adult female anogenital lichen sclerosus

Although it has been extensively used in the past, there appears to be no evidence base for the use of topical testosterone.[58,75–77] There is a solitary report of the effective use of topical progesterone.[78]

Although LS predominantly affects the genital region in female patients, suggesting a hormonal influence, neither pregnancy nor hormone replacement therapy seems to have any effect on the condition.

Male genital lichen sclerosus

Similarly, testosterone is no longer used.

Child anogenital lichen sclerosus

There is no supportive evidence for the use of topical oestrogens or testosterone in children.

Surgery, cryotherapy, photodynamic therapy, phototherapy, laser

Adult female anogenital lichen sclerosus

There is no indication for removal of vulval tissue in the management of uncomplicated LS, and surgery should be used exclusively for malignancy and postinflammatory sequelae.

In one small study of 12 patients with vulval LS and severe intractable itch, 75% obtained symptom relief with cryotherapy, 50% for 3 years[79] (*Strength of recommendation D; quality of evidence* 3).

In an open study of photodynamic therapy (PDT) for vulval LS (topical 5-aminolaevulinic acid, argon laser light, one to three treatments), 10 of 12 patients derived significant improvement[80] (*Strength of recommendation D; quality of evidence* 3). Another study demonstrated good symptomatic benefit in six of 10 patients treated with aminolaevulinic acid PDT using a bioadhesive patch.[81]

A single study of ultraviolet (UV) A1 in seven women with vulval LS that had not been controlled by topical steroids[82] reported initial improvement in five patients, although two relapsed and the others required ongoing treatment with topical steroids (*Strength of recommendation D; quality of evidence* 3).

Laser treatment, in a small study of 10 patients, was helpful symptomatically but did not stop the disease recurring. It was ineffective in one patient with urethral LS[83] (*Strength of recommendation D; quality of evidence* 3).

There is a solitary report of the beneficial use of focused ultrasound in 17 out of 31 cases of untreated LS using frequencies of 5–8 MHz[84] (*Strength of recommendation D; quality of evidence* 3).

Male genital lichen sclerosus

Although the first-line treatment for male patients with LS is a potent topical corticosteroid, it is not always successful when scarring has led to structural changes. The role of surgery for penile LS with symptoms due to persistent phimosis or meatal stenosis is supported with large studies documenting satisfactory results. In a multicentre series of 215 men with penile LS, and mean follow-up of almost 5 years, circumcision (indicated in 34 cases) was successful in 100%, meatotomy ($n = 15$) in 80%, circumcision and meatotomy ($n = 8$) in 100%, and various forms of urethroplasty ($n = 111$) in 73–91%.[85] LS is rare in the circumcised male, but circumcision does not always ensure protection against further flares of the disease. One series showed that 50% of men requiring circumcision continued to have lesions of LS,[19] and that the LS may Koebnerize in the circumcision scar. Koebnerization may be the explanation for the recurrence of urethral stricture, which is seen more frequently after surgery in patients with LS. This complication appears to be most common in those having a one-stage repair rather than stricture excision with a two-stage repair[86] (*Strength of recommendation D; quality of evidence* 3).

Laser treatment has been used to treat meatal stenosis,[83,87] but this is not standard practice. One study of 50 men with LS showed good long-term results after CO_2 laser treatment 13–19 years earlier, 80% having no evidence of LS[88] (*Strength of recommendation D; quality of evidence* 3). First-line treatment is urethral dilatation or formal meatoplasty. A topical steroid may be required at the same time as surgery.

Child anogenital lichen sclerosus

Surgical treatment of childhood phimosis by circumcision has demonstrated the presence of LS in a high proportion of cases. It is now being recognized that a trial of a topical steroid should be tried prior to circumcision in all cases of phimosis independent of aetiology and that circumcision should be reserved for treatment failures[70] (*Strength of recommendation D; quality of evidence* 3).

Extragenital LS

Shave (tangential) excision has been used,[89] and CO_2 laser has been reported to produce improvement in symptoms and appearance of lesions.

Various forms of phototherapy have been used for extragenital LS, including narrowband UVB, psoralen-UVA (PUVA) (alone or with topical tacrolimus) and UVA1. The latter appears to be the most successful in reducing clinical sclerosis as well as symptoms.[90–94] All of these treatments have only been reported as individual cases or small case series. One study compared the use of methyl aminolaevulinic acid pulsed dye laser (PDL)-mediated PDT vs. PDL alone on two areas of extragenital LS in one patient. The site treated with the PDT-PDL showed a slightly better response than the PDL alone[95] (*Strength of recommendation D; quality of evidence* 3).

Other treatments

Topical calcineurin inhibitors

The use of topical tacrolimus and pimecrolimus has been studied in women with vulval LS, after initial anecdotal reports and small series suggested benefit.[96–99] A study of 84 patients (49 women, 32 men and three girls) has supported the efficacy of tacrolimus.[100] A small study on the use of pimecrolimus in four prepubertal girls also noted an improvement in symptoms.[101] However, stinging on application was often reported. Furthermore, the long-term safety profile of these drugs is not established and there are concerns about an increased risk of neoplasia with their use in a disease with a premalignant potential.[102–104] There are case reports of SCC developing in patients who have been using these treatments[105,106] and longer-term studies are therefore of particular importance in LS. It is therefore recommended that the calcineurin inhibitors should not be used as first-line treatment (*Strength of recommendation D; quality of evidence* 3).

Ciclosporin, methotrexate and other immunosuppressive agents

A pilot trial of topical ciclosporin failed to have any beneficial clinical or histological effect in five cases of vulval LS.[107] However, oral ciclosporin was reported as effective in reducing symptoms and erosions in a series of five patients with refractory LS.[108]

Methotrexate has been used with success in an individual case of extragenital disease,[109] and hydroxycarbamide may also be an option for resistant LS[110] (*Strength of recommendation D; quality of evidence* 3).

There is a single study of the use of pulsed steroid and methotrexate which showed an improvement over 6 months[111] (*Strength of recommendation D; quality of evidence* 3).

Retinoids

Both topical and systemic retinoids have been used to treat LS.[112–114] There is no evidence that these are particularly effective in uncomplicated LS. However there is some evidence that they may have a role in hyperkeratotic and hypertrophic disease that does not respond to an ultrapotent steroid.

Potassium *para*-aminobenzoate

One report of five patients with LS at various sites, and resistant to numerous other therapies, documented good improvement with potassium *para*-aminobenzoate in all five (at quite wide dose ranges from 4 to 24 g daily, in divided doses)[115] (*Strength of recommendation D; quality of evidence* 3).

Others

There are reports of benefits from calcitriol, antimalarials, stanozolol, antipruritic and antihistamine agents, such as oxatomide, and various antibiotics (for which the main rationale is the uncertain link with *Borrelia* infection). These and others are summarized in reviews listed previously, but must all be viewed as less well-proven or anecdotal.[20–24]

Treatment failure

If treatment with topical corticosteroids appears to fail to bring LS under control then it is important to consider the following:

- Is noncompliance an issue? Sometimes patients may be alarmed at the contents of the package information insert warning against the use of topical corticosteroids in the anogenital area. Elderly patients disabled with poor eyesight and limited mobility may not be able to apply the medication appropriately.
- Has the correct diagnosis been made or is there an additional superimposed problem such as the development of a contact allergy to the medication, urinary incontinence, herpes simplex infection, intraepithelial neoplasia, malignancy, psoriasis or mucous membrane pemphigoid?
- Is there a secondary sensory problem? Has the LS been successfully treated, but the patient remains symptomatic because a secondary sensory problem (vulvodynia) has developed, or are there problems with intercourse which the individual feels too embarrassed to reveal?
- Is there a mechanical problem due to scarring, such as severe phimosis or meatal stenosis in males, in which case surgery may be indicated?

Follow-up

The risk of malignancy in uncomplicated genital LS that has been diagnosed and treated appropriately is very small. If malignancy occurs it tends to develop rapidly.

The authors suggest two follow-up visits after the initial consultation: one at 3 months to assess response to treatment and to ensure that the patient is using the topical corticosteroid appropriately and judiciously, and a second final assessment 6 months later to ensure that the patient is confident in treating their problem and to take the opportunity to discuss any residual problems that the patient might have before discharge back to the care of their primary physician. If patients continue to use a topical steroid it is suggested that they see their primary care physician once a year. Written instruction should be given to the patient at the time of their discharge from the clinic warning them that any persistent area of well-defined erythema, ulceration or new growth must be reported to their family practitioner straight away, who will then make an urgent referral back to an appropriate specialist. However, as over half of women discharged from U.K. vulval clinics are not subsequently followed up in primary care appropriately,[116] it is important that instructions for self-monitoring are fully understood.

Long-term follow-up in a secondary care specialist clinic is appropriate for patients with genital LS associated with troublesome symptoms, localized skin thickening, previous cancer or VIN, or pathological uncertainty about VIN.[117] The same advice is suggested for male patients with this problem. Biopsies of persistent ulcers, erosions, hyperkeratosis and fixed erythematous areas are advised to exclude intraepithelial neoplasia or invasive SCC. These patients usually have LS with a histological pattern that has features of both LS and LP with squamous cell hyperplasia. Clinically these patients seem to have an overlap syndrome and their disease runs a relentless course despite trials of various therapies, and a small percentage do go on to develop one or more SCCs.

Recommendations and conclusions

1 An ultrapotent topical corticosteroid is the first-line treatment for LS in either sex or age group, at any site, but there are no randomized controlled trials comparing steroid potency, frequency of application and duration of treatment.
2 Asymptomatic patients with evidence of clinically active LS (ecchymosis, hyperkeratosis and progressing atrophy) should be treated.

3 Anogenital LS is associated with SCC but the development of this complication is rare in clinical practice, < 5%. It is not yet known whether treatment lessens the long-term risk of malignant change.
4 Long-term follow-up in a specialized clinic is unnecessary for uncomplicated disease that is well-controlled clinically using small amounts of a topical corticosteroid, i.e. < 60 g in 12 months.
5 Secondary care follow-up should be reserved for patients with complicated LS that is unresponsive to treatment and those patients who have persistent disease with a history of a previous SCC.
6 A dermatology opinion should be sought in any patient with atypical or poorly controlled LS.
7 Surgical intervention is only indicated for the complications of scarring, premalignant change or an invasive SCC, in female patients. It may be useful in male patients with severe irreversible phimosis.
8 If psychosexual issues arise, these should be addressed and, if appropriate, referral made to a practitioner experienced in this field.

Audit points

1 Has a biopsy been performed in patients with clinically active LS that has not responded to treatment?
2 Are follow-up arrangements in place for patients with ongoing symptomatic disease?
3 Are patients with genital LS aware of the need to report any suspicious lesions within the affected skin?
4 Has a topical steroid of adequate potency and duration been used prior to circumcision in males with symptomatic LS?
5 Is histology always reported on male circumcision specimens?

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Appendix 1: Recommendation and evidence gradings

Level of evidence

Level of evidence	Type of evidence
1++	High-quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1+	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
1−	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias[a]
2++	High-quality systematic reviews of case–control or cohort studies. High-quality case–control or cohort studies with a very low risk of confounding, bias or chance and a high probability that the relationship is causal
2+	Well-conducted case–control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal
2−	Case–control or cohort studies with a high risk of confounding, bias or chance and a significant risk that the relationship is not causal[a]
3	Nonanalytical studies (e.g. case reports, case series)
4	Expert opinion, formal consensus

[a]Studies with a level of evidence '−' should not be used as a basis for making a recommendation. RCT, randomized controlled trial.

Strength of recommendation

Class	Evidence
A	• At least one meta-analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population, **or** • A systematic review of RCTs or a body of evidence consisting principally of studies rated as 1+, directly applicable to the target population and demonstrating overall consistency of results • Evidence drawn from a NICE technology appraisal
B	• A body of evidence including studies rated as 2++, directly applicable to the target population and demonstrating overall consistency of results, **or** • Extrapolated evidence from studies rated as 1++ or 1+
C	• A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results, **or** • Extrapolated evidence from studies rated as 2++
D	• Evidence level 3 or 4, **or** • Extrapolated evidence from studies rated as 2+, **or** • Formal consensus
D (GPP)	• A good practice point (GPP) is a recommendation for best practice based on the experience of the guideline development group

RCT, randomized controlled trial; NICE, National Institute for Health and Clinical Excellence.